PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
JOHN P. WHITE
COOPER & DUNHAM LLP
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 59597-E-PCT	Date of Mailing (*day/month/year*) 23 JAN 2003
International application No. PCT/US02/18684	FOR FURTHER ACTION See paragraphs 1 and 4 below
Applicant VIROLOGIC, INC.	International filing date (*day/month/year*) 04 June 2002 (04.06.2002)

1. ☐ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19: 2 MO ART 19 DUE. 3·23·03 - AP
The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34, chemin des Colombettes 3 MO IDS DUE 4·23·03
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet. (59597-E 59597-D, 59597-C, 59597-B, 59597-A, - AP

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90 *bis*.1 and 90 *bis*.3, respectively, before the completion of the technical preparations for international publication. 12·4·03 - AP

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices. 1·4·03 - AP 2·4·03 - AP

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US Commissioner for Patents Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Sharon Foley Telephone No. (703) 308-0196

Form PCT/ISA/220 (April 2002) *(See notes on accompanying sheet)*

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 59597-E-PCT/	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US02/18684	International filing date (*day/month/year*) 04 June 2002 (04.06.2002)	(Earliest) Priority Date (*day/month/year*) 04 June 2001 (04.06.2001)
Applicant VIROLOGIC, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the Report**
   a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
   ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:
   ☐ contained in the international application in written form.
   ☐ filed together with the international application in computer readable form.
   ☐ furnished subsequently to this Authority in written form.
   ☐ furnished subsequently to this Authority in computer readable form.
   ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
2. ☐ **Certain claims were found unsearchable** (See Box I).
3. ☒ **Unity of invention is lacking** (See Box II).
4. With regard to the title,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established by this Authority to read as follows:
5. With regard to the abstract,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is Figure No. ____
   ☐ as suggested by the applicant.
   ☐ because the applicant failed to suggest a figure.
   ☐ because this figure better characterizes the invention.
   ☒ None of the figures

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/18684

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-12

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/18684

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/18, 1/68, 1/70
US CL : 435/5, 6, 32

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/5, 6, 32

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ZIERMANN et al. A mutation in human immunodeficiency virus type 1 protease, N88S, that causes in vitro hypersensitivity to amprenavir. J. Virology. May 2000. Vol 74. No. 9, pages 4414-4419, especially pages 4415-4416.	1-12

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
12 December 2002 (12.12.2002)

Date of mailing of the international search report
23 JAN 2003

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
Facsimile No. (703)305-3230

Authorized officer
Sharon Foley

Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-12, drawn to a method of assessing the effectiveness of protease antiretroviral therapy in an HIV-infected subject by evaluating the presence of a mutation at codon 88.

Group II, claim(s) 13-16, drawn to a method of evaluating the effectiveness of an HIV antiretroviral drug candidate with a vector encoding a mutation at codon 88.

Group III, claim(s) 17-20, drawn to a resistance test vector comprising an HIV patient-derived segment having a mutation at codon 88.

Group IV, claim(s) 21, drawn to a method for evaluating the viral fitness of a patient's virus.

Group V, claim(s) 22-44, 80-85, 98-113, 117-120, drawn to a method of evaluating the effectiveness of an HIV antiretroviral drug candidate with a vector encoding a mutation at codon 82.

Group VI, claim(s) 45-67, 80-85, 98-120, drawn to a method of evaluating the effectiveness of an HIV antiretroviral drug candidate with a vector encoding a mutation at codon 90.

Group VII, claim(s) 68-70, drawn to a method of evaluating the effectiveness of an HIV antiretroviral drug candidate with a vector encoding a mutation at codon 82 and 90.

Group VIII, claim(s) 71, 72, and 86, drawn to a method of evaluating the effectiveness of an HIV antiretroviral drug candidate with a vector encoding a mutation at codon 82.

Group IX, claim(s) 73, 74, and 86, drawn to a method of evaluating the effectiveness of an HIV antiretroviral drug candidate with a vector encoding a mutation at codon 90.

Group X, claim(s) 74 and 75, drawn to a method of evaluating the effectiveness of an HIV antiretroviral drug candidate with a vector encoding a mutation at codon 82 and 90.

Group XI, claim(s) 76, 77, 87-91, 121, and 122, drawn to a resistance test vector comprising an HIV patient-derived segment having a mutation at codon 82.

Group XII, claim(s) 78, 87-91, 121, and 122, drawn to a resistance test vector comprising an HIV patient-derived segment having a mutation at codon 90.

Group XIII, claim(s) 79 and 92-97, drawn to a method for determining the replication capacity for a patient's virus.

Group XIV, claim(s) 123 and 125, drawn to a method for determining whether a patient's virus, comprising a mutation at codon 30, is resistant to protease inhibitor drugs.

Group XV, claim(s) 124, drawn to drawn to a method for determining whether a patient's virus is resistant to protease inhibitor drugs.

Group XVI, claim(s) 126, drawn to drawn to a method for determining whether a patient's virus, comprising a mutation at codon 50, is resistant to protease inhibitor drugs.

INTERNATIONAL SEARCH REPORT

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The inventions listed as Groups I-XVI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature of group I is drawn to a method of assessing the effectiveness of an antiretroviral therapy by evaluating whether an HIV sample comprises a mutation at codon 88. Any subsequent group that does not share this special technical feature lacks unity of invention with the first group.

The special technical feature if group II is drawn to a method of evaluating the effectiveness of an HIV antiretroviral drug candidate with a vector encoding a mutation at codon 88. This group does not share the special technical feature with group I because the groups comprise different method steps and ingredients.

The special technical feature if group III is drawn to a first product, a vector encoding a mutation at codon 88. This group does not share the special technical feature with group I because the product is not required to practice the method of group I.

The special technical feature of group IV is a method of evaluating the viral fitness of a patient's virus. This group does not share the special technical feature with group I because the method steps are different from the method of group I and requires different ingredients.

The special technical feature of group V is drawn to a method of assessing the effectiveness of an antiretroviral therapy by evaluating whether an HIV sample comprises a mutation at codon 82. This group does not share the special technical feature with group I because the method steps are drawn to evaluating a different sequence that distinguishes the special technical feature in group I.

The special technical feature of group VI is drawn to a method of assessing the effectiveness of an antiretroviral therapy by evaluating whether an HIV sample comprises a mutation at codon 90. This group does not share the special technical feature with group I because the method steps are drawn to evaluating a different sequence that distinguishes the special technical feature in group I.

The special technical feature of group VII is drawn to a method of assessing the effectiveness of an antiretroviral therapy by evaluating whether an HIV sample comprises a mutation at codon 82 and 90. This group does not share the special technical feature with group I because the method steps are drawn to evaluating a different sequence that distinguishes the special technical feature in group I.

The special technical feature if group VIII is drawn to a method of evaluating the effectiveness of an HIV antiretroviral drug candidate with a vector encoding a mutation at codon 82. This group does not share the special technical feature with group I because the groups comprise different method steps and ingredients.

The special technical feature if group IX is drawn to a method of evaluating the effectiveness of an HIV antiretroviral drug candidate with a vector encoding a mutation at codon 90. This group does not share the special technical feature with group I because the groups comprise different method steps and ingredients.

The special technical feature if group X is drawn to a method of evaluating the effectiveness of an HIV antiretroviral drug candidate with a vector encoding a mutation at codon 82 and 90. This group does not share the special technical feature with group I because the groups comprise different method steps and ingredients.

The special technical feature if group XI is drawn to a second product, a vector encoding a mutation at codon 82. This group does not share the special technical feature with group I because the product is not required to practice the method of group I.

The special technical feature if group XII is drawn to a third product, a vector encoding a mutation at codon 90. This group does not share the special technical feature with group I because the product is not required to practice the method of group I.

The special technical feature of group XIII is a method for determining the replication capacity of a patient's virus. This group does not share the special technical feature with group I because the method steps are different from the method of group I and requires different ingredients.

The special technical feature of group XIV is drawn to a method of determining whether an HIV virus is resistant to a protease inhibitor drug by determining whether the sample has a mutation at codon 30 exists. This group does not share the special technical feature with group I because the method steps and ingredients to practice each of the methods is distinctly different.

The special technical feature of group XV is drawn to a method of determining whether an HIV virus is resistant to a protease inhibitor drug by determining whether the sample is resistant to any one protease inhibitor drug. This group does not share the special technical feature with group I because the method steps and ingredients to practice each of the methods is distinctly different.

The special technical feature of group XVI is drawn to a method of determining whether an HIV virus is resistant to a protease inhibitor drug by determining whether the sample has a mutation at codon 50 exists. This group does not share the special technical feature with group I because the method steps and ingredients to practice each of the methods is distinctly different.

Only claims 1-12 will be searched if applicant does not agree to pay for any additional groups.

INTERNATIONAL SEARCH REPORT

PCT/US02/18684

Continuation of B. FIELDS SEARCHED Item 3:
USPatfull, USPGpub, EPO, JPO, Derwent, medline, embase, biosis
search terms: amprenavir, 88, resist, codon, HIV, mutat

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty and of the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended ?

The claims only.

The description and the drawings may only be amended during international preliminary examination under Chapter II.

When ? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How ? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

What documents must/may accompany the amendments ?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confounded with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

(i) the claim is unchanged;
(ii) the claim is cancelled;
(iii) the claim is new;
(iv) the claim replaces one or more claims as filed;
(v) the claim is the result of the division of a claim as filed.

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
JOHN P. WHITE
COOPER & DUNHAM LLP
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

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NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

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Applicant VIROLOGIC, INC.	

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Form PCT/ISA/220 (April 2002)

(See notes on accompanying sheet)